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Award Number: DAMD17-95-2-5012

TITLE: Postdoctoral Research Associateship Program with USAMRMC

PRINCIPAL INVESTIGATOR: Judith Nyquist, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

REPORT DATE: February 2003

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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20030416 258

REPORT DOCUMENTATION PAGE

Form Approved
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Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE February 2003	3. REPORT TYPE AND DATES COVERED Final (4 Sep 95 - 28 Feb 03)	
4. TITLE AND SUBTITLE Postdoctoral Research Associateship Program with USAMRMC			5. FUNDING NUMBERS DAMD17-95-2-5012	
6. AUTHOR(S): Judith Nyquist, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) National Academy of Sciences Washington, DC 20418 Email: jnyquist@nas.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) none provided				
14. SUBJECT TERMS: research candidates				15. NUMBER OF PAGES 31
				16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified		20. LIMITATION OF ABSTRACT Unlimited

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THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

National Research Council RESEARCH ASSOCIATESHIP PROGRAM

with the

**U.S. Army Medical Research Materiel Command
(AMRMC)**

Contract number: DAMD17-95-2-5012

Publicity

The National Academies Research Associateship Programs for the report period were announced to the scientific community in the fall of the preceding year, 2001. Publicity materials describing the National Research Council-U.S. Army Medical Research Materiel Command (AMRMC). Programs were distributed in November to presidents, graduate deans, and heads of appropriate science and engineering departments and minority-affairs offices of all academic degree-granting institutions in the United States. An e-mail announcement of the programs was sent to these same contact points prior to each review deadline. Promotional materials were sent to Laboratory Program Representatives, Associateship Advisers, and other interested persons. General advertisements of programs were placed in leading scientific and engineering publications. Publicity materials and other related information were made available on the internet. Research Associateship Programs staff attended numerous society meetings and minority recruitments to promote the various programs and meet with prospective applicants throughout the year.

Requests

Application materials were distributed in response to specific requests for information about the AMRMC Research Associateship Program or as a result of general requests by persons whose fields of specialization appeared to be appropriate for the research opportunities available in the AMRMC laboratories.

Competition

Panel reviews of applicants for the Research Associateship Programs, including those with the U.S. Army Medical Research Materiel Command, are conducted in winter, spring, summer, autumn of each year. The following is a breakdown of the action taken with the applications during the report period.

	review-year <u>winter -02</u>	<u>autumn- 02</u>	<u>spring- 03</u>	<u>TOTAL</u>
TOTAL APPLICATIONS				
Number of Applications Reviewed	4	12	12	28
Applications not recommended (did not pass Review)	2	1	1	4
Applications Recommended (passed Review)	2	11	11	24
Awards offered	0	9	0	9
Awards accepted	0	5	0	5
Awards declined	0	3	0	3
Awards withdrawn by RAP (NRC officially withdrew award <i>after</i> it had been accepted.)	0	1	0	1

Associates' Citizenship

Associates on tenure between **10/1/2002** and **2/28/2003** were citizens or Permanent Residents of the United States and the following countries:

2 Australia	1 Italy
1 Bangladesh	3 People's Republic of China
1 Denmark	1 Poland
1 Hungary	4 Russia
4 India	1 Ukraine
1 Israel	25 United States

Associates' Activities

Associates who ended tenure during the report period were on tenure for an average of **29** months, ranging from **24** months to **39** months.

Of the **5** Associates who ended tenure during the report period, **4 (80%)** submitted final reports. In the final reports, Associates indicated the following scholarly activity while on tenure.

7 Articles published in refereed journals	4 International presentations
1 Patent applications	10 Domestic presentations
	1 Awards

After ending their tenure, Associates indicated their future plans as follows:

2 Remain at host agency as perm. employee	- Research/teaching-foreign college/university
- Remain at host agency as contract employee	- Research/admin in industry
- Research position at other US gov't. lab	- Research/admin in non-profit organization
- Administrative position at US gov't. lab	- Postdoctoral research
- Research position at foreign gov't. lab	1 Self employed
- Research/teaching-US college/university	1 Other (may include unemployed)

In their final reports, Associates were asked to evaluate certain aspects of their experiences on a scale of 1 (low) to 10 (high). The average rating for each item follows:

-	<i>Short-term value:</i>	Development of knowledge, skills, and research productivity
-	<i>Long-term value:</i>	How your Research Associateship affected your career to date
8.5	<i>Laboratory:</i>	Quality of the support you received from the federal laboratory
9.8	<i>RAP:</i>	Quality of the support you received from the Research Associateship Programs

Advisers also were asked to complete an evaluation of the Associate. The following summarizes the Adviser evaluations for Associates ending tenure during the report period. Of the **5** Associates who ended tenure, **2 (40%)** Adviser evaluations were completed. Assessments were made on six criteria using the following rating scale: 1-below average, 2-average, 3-above average, 4-good, and 5-outstanding/exceptional. The average rating for each item follows:

3.0 Knowledge of field	3.0 Independence
3.0 Innovative thinking	3.0 Motivation
2.5 Research techniques	3.0 Overall scientific ability

The Adviser was asked, "Would you like this Associate as a professional colleague?" The Advisers responded in the following manner:

1	Yes	-	No Comment
1	No	-	No Answer

Additional information about the Associates' activities can be found in the attachments described below and the Appendix.

Attachment 1: Associates who were on tenure between **10/1/2002** and **2/28/2003**. Included are the Associate's laboratory center/division location, the starting and termination dates, and the names of their advisers. For those Associates who ended tenure during the report period, it is noted if the final and adviser evaluation reports have been received. Associates are required to submit final reports upon termination of tenure, and advisers are asked to submit a final evaluation of each Associate. Associates who have not submitted a final report have received follow-up correspondence.

Attachment 2: All recommended candidates by category (e.g., Recommended, Accepted, No Funding, Declined, etc.). This report includes information about citizenship, Ph.D. institution, title of proposed research, proposed or actual starting date, and adviser.

Attachment 3: Summaries of Associate patent activity, if any, and Associate research during tenure as reported on the Associates' termination reports. The summary of patent activity includes the patent application title, inventor(s), and date of application.

Appendix: Final reports received from the Associates who ended tenure during the report period.

Associates On Tenure**10/1/2002 - 2/28/2003****Attachment 1****AMRMC - U.S. Army Medical Research Institute of Chemical Defense**

3/26/2003 Page 1 of 4

Associate Name+ Adviser	Division	Tenure Dates Start/End	Termination Report	Adviser Report
Petrikovics, Ilona <i>Dr. Steven I. Baskin</i>	(S) Pharmacology Division	1/3/2003 - 1/2/2004		

1 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Highlighted entries indicate no entry on the Award Init Screen but data on the Post Tenure Screen.

Associates On Tenure**10/1/2002 - 2/28/2003****Attachment 1****AMRMC - U.S. Army Medical Research Institute of Infectious Diseases**

3/26/2003 Page 2 of 4

Associate Name+ Adviser	Division	Tenure Dates Start/End	Termination Report	Adviser Report
Keller, Michael Anthony <i>Dr. Alan L. Schmaljohn</i>	Virology Division	12/9/2002 - 12/8/2003		

1 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Highlighted entries indicate no entry on the Award Init Screen but data on the Post Tenure Screen.

Associates On Tenure**10/1/2002 - 2/28/2003****Attachment 1****AMRMC - U.S. Army Research Institute of Environmental Medicine**

3/26/2003 Page 3 of 4

Associate Name+ Adviser	Division	Tenure Dates Start/End	Termination Report	Adviser Report
Weyand, Peter Gregory <i>Dr. Reed W. Hoyt</i>	(S) Divison not specified	9/20/1999 - 12/31/2002	Not Recd	Not Recd

1 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Highlighted entries indicate no intry on the Award Init Screen but data on the Post Tenure Screen.

Associates On Tenure**10/1/2002 - 2/28/2003****Attachment 1****AMRMC - Walter Reed Army Institute of Research**

3/26/2003 Page 4 of 4

Associate Name+ Adviser	Division	Tenure Dates Start/End	Termination Report	Adviser Report
Chen, Yue-Qin <i>Dr. Peter K. Chiang</i>	(S) Division Of Experimental Therapeutics	2/11/2003 - 2/10/2004		
Fleming, Sherry D. <i>Dr. George C. Tsokos</i>	Division Of Medicine	1/2/2001 - 1/1/2003	Received	Not Recd
Leader, Haim Nissan <i>Dr. Richard K. Gordon</i>	(S) Division Of Biochemistry	11/4/2002 - 5/3/2003		
Miroshnikova, Olga Vyatcheslavovna <i>Dr. Ai J. Lin</i>	Division Of Experimental Therapeutics	2/25/2003 - 2/24/2004		
Nair, Lalitha Punchayil Velayudhan <i>Dr. David E. Lanar</i>	(S) Division Of Commun Diseases/Immunology	0/11/2000 - 10/10/2000	Received	Not Recd
Savransky, Vladimir <i>Dr. Jeenan Tseng</i>	(S) Division Of Pathology	2/12/2001 - 2/11/2003	Received	Received
Thakur, Suman Siddharth <i>Dr. Bhupendra P. Doctor</i>	Division Of Biochemistry	1/18/2002 - 11/17/2000		
Zhu, Shuren <i>Dr. Ai J. Lin</i>	Division Of Experimental Therapeutics	11/1/1999 - 10/31/2002	Received	Received

8 Associates Listed

*** End of Center ***

+ (S) indicates the associate was a Senior.

Highlighted entries indicate no entry on the Award Init Screen but data on the Post Tenure Screen.

Recommended Candidates 10/1/2002 - 2/28/2003
AMRMC- U.S. Army Institute of
Surgical Research

Attachment 2

3/26/2003 Page 1 of 7

February 2003

1- Recommended

WENKE, JOSEPH C

Ph.D. Date: 2003

Citizenship: United States

Texas A&M University

Adviser: Dr. Victor A. Convertino

Research Field: Physiology

Research Title: Antimicrobial Bone Graft Substitutes

* * *

Recommended Candidates 10/1/2002 - 2/28/2003
AMRMC- U.S. Army Medical
Research Institute of Chemical
Defense

Attachment 2

3/26/2003 Page 2 of 7

October 2002

A- Accepted Award

LANGSTON, JEFFREY L	Ph.D. Date: 2002
Citizenship: United States	Auburn University/AL
Adviser: Dr. Maurice L. Sipos	Expected Starting Date: 5/05/03
Research Field: Neurotoxicology	Termination Date: 5/04/04
Research Title: Development of a Guinea Pig Test Battery to Assess the Behavioral Effects of Exposure to Chemical Warfare Nerve Agents	

February 2003

1- Recommended

JUNG, BRUCE J	Ph.D. Date: 2000
Citizenship: United States	University of Florida
Adviser: Dr. Tsung-Ming A. Shih	
Research Field: Neurotoxicology	
Research Title: Effects of Repeated Low Dose VX Exposure on Neurobehavior, EEG Spectrum, and Extracellular Neurotransmitter Levels	

* * *

Recommended Candidates 10/1/2002 - 2/28/2003
AMRMC- U.S. Army Medical
Research Institute of Infectious

Attachment 2

3/26/2003 Page 3 of 7

Diseases

October 2002

1- Recommended

RHOADES, ELIZABETH R
Citizenship: United States
Adviser: Dr. Sina Bavari
Research Field: Immunology
Research Title: Identification of Human MHC Class II-Restricted Epitopes of the Protective antigen (PA) and Novel Correlates of Immunity

Ph.D. Date: 1997
Colorado State University

A- Accepted Award (2 Applicants listed)

FRITZ, ELIZABETH A
Citizenship: United States
Adviser: Dr. Peter B. Jahrling
Research Field: Virology
Research Title: Modulation of the Immune Response During Smallpox and Monkeypox Infections

Ph.D. Date: 2002
Rush University/IL
Actual Starting Date: 3/03/03
Termination Date: 3/02/04

KELLER, MICHAEL A
Citizenship: United States
Adviser: Dr. Alan L. Schmaljohn
Research Field: Virology
Research Title: Therapeutic Targeting of Filovirus RNA-Dependent RNA Polymerase

Ph.D. Date: 2002
Wake Forest University/NC
Actual Starting Date: 12/09/02
Termination Date: 12/08/03

8- Declined (3 Applicants listed)

ELLISON, MICHAEL A
Citizenship: United States
Adviser: Dr. Leonard A. Smith
Research Field: Biochemistry
Research Title: Development of Vaccines Against Botulinum Neurotoxin Type G

Ph.D. Date: 2002
University of Utah

GARRUS, JENNIFER E
Citizenship: United States
Adviser: Dr. Sina Bavari
Research Field: Virology
Research Title: Late Domain Mediated Filovirus Budding

Ph.D. Date: 2002
University of Utah

MARIANS, RUSSELL C
Citizenship: United States
Adviser: Dr. Bradford Powell
Research Field: Bacteriology
Research Title: Characterizing the Immune Response to the F1-V Y.Pestis Vaccine

Ph.D. Date: 2001
Mt Sinai School of Medicine-CUNY

**AMRMC- U.S. Army Medical
Research Institute of Infectious**

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Diseases

1- Recommended (6 Applicants listed)

Ph.D. Date: 2003
U of North Carolina-Chapel Hill

Ph.D. Date: 1999
University of South Alabama

Ph.D. Date: 2002
State U of New York-Stony Brook

Ph.D. Date: 2003
University of Notre Dame/TN

Ph.D. Date: 2003
Virginia Polytech Inst & State U

Ph.D. Date: 2003
Brown University/RI

* * *

Recommended Candidates 10/1/2002 - 2/28/2003
AMRMC- U.S. Army Research
Institute of Environmental
Medicine

Attachment 2

3/26/2003 Page 5 of 7

February 2003

1- Recommended

JAY, OLIVER E

Ph.D. Date: 2002

Citizenship: England, U.K.

Loughboro U Tech

Adviser: Dr. John W. Castellani

Research Field: Physiology and Biophysics

Research Title: Predicting Operational Performance During Cold Water Immersion

* * *

KONGKASURIYACHAI, DARIN
 Citizenship: Thailand
 Adviser: Dr. Jetsumon P. Sattabongkot
 Research Field: Infectious Diseases
 Research Title: Molecular Mechanism of Relapsing Malaria: Identification of Hypnozoite Stage Antigens by Differential Display

Ph.D. Date: 2003
 Johns Hopkins University/MD

Recommended Candidates 10/1/2002 - 2/28/2003
AMRMC- Walter Reed Army
Institute of Research

Attachment 2

3/26/2003 Page 7 of 7

February 2003

1- Recommended

SILMAN, HARRY I

Citizenship: Israel

Adviser: Dr. Bhupendra P. Doctor

Research Field: Biochemistry

Research Title: Crystallization and Structure Determination of a Native Cholinesterase Tetramer

Ph.D. Date: 1964

Weizmann Inst of Science/Israel

* * *

**Summary of
Associate Research**

10/1/2002 - 2/28/2003

Attachment 3
3/26/2003 Page 1 of 2

AMRMC- U.S. Army Medical Research and Materiel Comm:

Fleming, Sherry D.

1/02/2001 1/01/2003

- 1 Complement inhibitors can prevent local and systemic injury due to mesenteric ischemia/reperfusion (IR).
- 2 The anaphylotoxin C5a is critical for both local and systemic tissue damage.
- 3 The classical complement pathway is activated by natural antibodies in response to IR-induced damage.
- 4 IgM and IgG natural antibodies each contribute unique aspects of the tissue damage.
- 5 The natural antibody repertoire is altered in the absence of complement receptor 2 (CR2).

Nair, Lalitha Punchayil Velayudhan

10/11/2000 10/10/2002

- 1 Worked in the development of the purification of an important malaria vaccine target antigen PfAMA/E that (99% pure) was scaleable and transferable to GMP facility, and that induced high titre growth inhibitory antibodies in rabbits.
- 3 Purification protocol was used in the writing of Batch Production Record BPR-480, entitled "Preparation of a Bulk Lot Recombinant P. falciparum AMA1/E Protein Expressed in Escherichia coli, Origami Strain."
- 5 The data from this analysis will be part of an IND application to the FDA to use this protein as a vaccine in humans.
- 7 Cloned, expressed, purified and immunologically characterized all six subdomain constructs from ectodomain of AMA-1 in bacteria. It enabled to fine map the immunodominant regions of the whole molecule.
- 9 Erythrocyte binding activity of AMA-1 and the subdomain fragments is established from this study. This data may help to develop better AMA-1 based constructs for vaccine study.

Savransky, Vladimir

2/12/2001 2/11/2003

- 1 Developing the new murine intranasal SEB toxic shock model.
- 2 Screening various SEB mutant proteins for superantigenicity, toxicity, and selecting safe mucosal vaccine candidate.

AMRMC- U.S. Army Medical Research and Materiel Comm:

3 Studying immunogenicity and protective properties of selected candidates.

4 Developing a novel mucosal vaccine against SEB intoxication.

Zhu, Shuren

11/01/1999 10/31/2002

1 A novel class of peptidomimetic antimalarial agents has been discovered.

2 Compounds exhibited potent in vitro and in vivo activity against malarial parasites.

FINAL REPORT

Enter information electronically in Layout view.

Return this form directly to the NRC as an E-mail attachment, or print out and mail or fax.

1) Associate Last or Family Name Fleming		First Name Sherry	M.I. D
2) FORWARDING Address (for tax statement / final stipend check) 11503 Regnid Dr. Silver Spring, MD 20902		FORWARDING Phone(s) and E-Mail (if known) phone: (301) 319-7359 phone: (301) 942-9440 e-mail: sfleming@usuhs.mil	
3) Today's Date		Dates of Tenure from January 2, 2001 to January 1, 2003	
4) Agency AMRMC	Laboratory WRAIR/Tsokos	or NASA Ctr	Division / Branch / Directorate Cellular Injury/MCR
5) NAME OF RESEARCH ADVISER George Tsokos			

6) TITLE OF RESEARCH PROPOSAL

Role of natural antibodies and complement inhibitors in mesenteric ischemia-reperfusion injury

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Complement inhibitors can prevent local and systemic injury due to mesenteric ischemia/reperfusion (IR)
- 2) The anaphylotoxin C5a is critical for both local and systemic tissue damage
- 3) The classical complement pathway is activated by natural antibodies in response to IR-induced damage.
- 4) IgM and IgG natural antibodies each contribute unique aspects of the tissue damage.
- 5) The natural antibody repertoire is altered in the absence of complement receptor 2 (CR2).

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

I am continuing the CR2 studies to determine the antigen for the natural antibody recognition of ischemic tissue. In addition, the cell type that is secreting the natural antibodies and the recruitment of these cells to the local area are being investigating. The C5 project is being extended to determine the actual involvement of integrin $\alpha 4$ and VCAM in local and systemic injury.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Fleming, S.D., Lambris, J.D., T.Shea-Donohue and G.C. Tsokos. 2002. C5 is critical for the mesenteric ischemia/reperfusion-induced local and remote organ injury. 2002. Clinical Immunol. In Press.

Fleming, S.D., T.Shea-Donohue, J.M. Guthridge, L. Kulik, T.J. Waldschmidt, M.G. Gipson, G.C. Tsokos and V.M. Holers. 2002. Mice deficient in complement receptors 1 and 2 lack a tissue injury-inducing subset of the natural antibody repertoire. J. Immunol. 169:2126-2133.

Fleming, S.D., B. Starnes, J.G. Kiang, A. Stojadinovic, G.C. Tsokos, and T.Shea-Donohue. 2002. Heat stress protection against mesenteric ischemia/reperfusion-induced alterations in intestinal mucosa in rats. J. Applied Physiol. 92:2600-2607.

Rehrig, S., S.D. Fleming, J. Anderson, J.M. Guthridge, J. Rakstang, C. McQueen, V.M. Holers, G.C. Tsokos, and T.Shea-Donohue. 2001. Complement inhibitor, Crry-Ig attenuates intestinal damage after the onset of mesenteric ischemia/reperfusion injury in mice. J. Immunol. 167: 5921-5927.

b) Books, book chapters, other publications

Fleming, S.D. and G.C. Tsokos. 2001. Complement Inhibitors in Rheumatic Diseases in Modern therapeutics in Rheumatic Diseases. Pg 443-452. Ed. G.C. Tsokos, Humana Press, Totowa, NJ.

c) Manuscripts in preparation, manuscripts submitted

Karpel-Massler, G., Fleming, S.D., Kirschfink, M., Tsokos, G.C. 2002. Human C1 esterase inhibitor attenuates murine mesenteric ischemia/reperfusion induced local organ injury. Submitted. 2002.

Fleming, S.D., Lambris, J.D., and G. Tsokos. C5a-mediated mesenteric ischemia/reperfusion injury is independent of polymorphonuclear neutrophils.

Fleming, S.D., Anderson, J., Rehrig, S., Wilson, F., Shea-Donohue, T., and G. Tsokos. Systemic effects of Crry-Ig after mesenteric ischemia/reperfusion.

Anderson, J. Fleming, S.D., Rehrig, S., Tsokos, G., Shea-Donohue, T and M. Basta. Intravenous immunoglobulin attenuates mesenteric ischemia-reperfusion injury

10 *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

None

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

International Complement Society Meeting, Palermo, Italy, Sept. 2002. Fleming, SD, Lambris, JD, Shea-Donohue, T, and Tsokos, GC. C5a is responsible for the mesenteric ischemia/reperfusion-induced local and remote organ injury. Poster Preseentation

International Complement Associated Disease, Animal Models and Therapeutic Workshop. Santorini, Greece. 2001. Fleming, SD, Lambris, JD, Shea-Donohue, T. and Tsokos, GC. C5a is responsible for the mesenteric ischemia/reperfusion-induced local and remote organ injury Abstract #20. Oral Presentation.

Domestic

AAATAC meeting, Florida, Sept. 2002, Oral Presentation.

AAATAC meeting, Florida, Sept. 2001

The C5a fragment of C5 is critical of the mesenteric ischemia/reperfusion-induced local and remote organ injury, Fleming, SD, Lambris, JD, Shea-Donohue, T and Tsokos, GC.

FOCIS Meeting, Boston, MA, 2001 Poster Presentation

C5 inhibitors prevent mesenteric ischemia/reperfusion induced injury. by Fleming, SD, Lambris, JD, Shea-Donohue, T. and Tsokos, GC. Clinical Immunology 99:175 Abstract #221.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

Research seminar. Dept. Pathology and Laboratory Medicine, Univ. Penn, Philadelphia, PA. March 2002

Immunology section, 4 lectures, Structure and Function of Organ Systems, Uniformed Services University of the Health Sciences, Bethesda, MD April 2002.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

None

14) *POST-TENURE POSITION TITLE*

CRM Investigator

15) *POST-TENURE ORGANIZATION* Provide name and city of organization.

Clinical Research Management
Silver Spring, MD 20910

16) *POST-TENURE POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|--|--|
| <input type="checkbox"/> Remain at Host Agency as Permanent Employee | <input type="checkbox"/> Research/Teaching at US College/University |
| <input checked="" type="checkbox"/> Remain at Host Agency as Contract/Temporary Employee | <input type="checkbox"/> Research/Teaching at Foreign College/University |
| Abbreviate Host Laboratory/Center <u>WRAIR</u> | <input type="checkbox"/> Research/Administration in Industry |
| <input type="checkbox"/> Research Position at Another US Government Laboratory | <input type="checkbox"/> Research/Admin in Non-Profit Organization |
| <input type="checkbox"/> Administrative Position at US Government Laboratory | <input type="checkbox"/> Postdoctoral Research |
| <input type="checkbox"/> Research Position at Foreign Government Laboratory | <input type="checkbox"/> Self Employed |
| | <input type="checkbox"/> Other: specify _____ |

17) *APPRAISAL OF THE ASSOCIATESHIP PROGRAM* Please rate each of the following

Your experience as a NRC Research Associate in this federal Laboratory 1 (poor) to 10 (excellent)

10 Short-term value: development of knowledge, skills, and research productivity

Comments:

10 Long-term value: how your NRC Associateship award affected your career to date
Comments:

Administrative Support 1 (poor) to 10 (excellent)

9 Quality of the support you received from the federal Laboratory

10 Quality of the support you received from the NRC staff (Leave blank, if not applicable - e.g., NIST)

Comments on both/either:

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT

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THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

National Research Council Associateship Programs

FINAL REPORT

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Return this form directly to the NRC as an E-mail attachment, or print out and mail or fax.

1) Associate Last or Family Name		First Name	M.I.
Nair		Lalitha	PV
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F 62, CSIR Scientist Apartment, Maharani Bagh, New Delhi 110065, India		Phone: 91-11-6917555 Phone: 91-11-6325129 E-mail: Lalithapv@hotmail.com	
3) Today's Date		Dates of Tenure	
September 24, 2002		from October 11, 2000 to October 10, 2002	
4) Agency	Laboratory or NASA Center	Division / Branch / Directorate	
AMRMC	WRAIR	CD & I, Immunology	

5) NAME OF RESEARCH ADVISER

David E Lanar

6) TITLE OF RESEARCH PROPOSAL

Cloning, Expression and Immunological Characterization of AMA-1 and its Subdomain Fragments in Bacteria

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Worked in the development of the purification of an important malaria vaccine target antigen PfAMA1/E that (99% pure) was scaleable and transferable to GMP facility, and that induced high titre growth inhibitory antibodies in rabbits.
- 2) Purification protocol was used in the writing of Batch Production Record BPR-480, entitled "Preparation of a Bulk Lot Recombinant P. falciparum AMA1/E Protein Expressed in Escherichia coli, Origami Strain.
- 3) The data from this analysis will be part of an IND application to the FDA to use this protein as a vaccine in humans.
- 4) Cloned, expressed, purified and immunologically characterized all six subdomain constructs from ectodomain of AMA-1 in bacteria. It enabled to fine map the immunodominant regions of the whole molecule.
- 5) Erythrocyte binding activity of AMA-1 and the subdomain fragments is established from this study. These data may help to develop better AMA-1 based constructs for vaccine study.

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Cloned and expressed all the six subdomain fragments of AMA-1 ectodomain in bacteria, purified in order to fine map the immune responses. The purified double domains have generated high titre antibodies in rabbits that recognized the native parasite in IFA and recognized the parasite AMA-1 in Western blot experiments. Domain I+II generated most of the growth inhibitory antibodies on a growth inhibition/invasion assay in vitro, suggesting that this region is most important in AMA-1 ectodomain. Also, most of the immune responses towards the ectodomain are localized in the domain II, though this region alone is not enough to generate inhibitory antibodies. AMA-1 and all six subdomains, I+II, II+III, I+III, I, II and III have shown to have erythrocyte binding activity to human RBC. Immunization with single domains is being done. Projects on D I+II crystal structure elucidation and mapping of monoclonal antibodies are also in progress, in collaboration.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

1. Purification and characterisation of the refolded ectodomain of the Apical Membrane Antigen-1 of Plasmodium falciparum expressed in Escherichia coli. S Dutta, P V Lalitha, L A Ware, A Barbosa, JK Moth, MA Vassel, S Kitov, N Kolodny, J D Haynes and D E Lanar, Infection and Immunity, 2002, 70(6), 3001-10.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

1. Lalitha PV, Ware LA, Barbosa A, Dutta S, Moch K, Haynes JD, Lanar DE. Protective antibody responses to AMA-1 is directed towards D I+II: Results from Analysis of Cloning, expression, purification and immunological characterisation of refolded Plasmodium falciparum AMA-1 Subdomain fragments in E. coli.

10 *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

1. Process for purification of recombinant Plasmodium falciparum AMA-1 from E. coli . D E Lanar, S Dutta, L A Ware and Lalitha P V. Filed a Provisional U.S. Patent Application, filing date: March 26, 2001.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

1. Barbosa A, Wood CL, Lalitha PV, Tighe JJ, Ware LA, Dutta S, Haynes JD, Moch JK, Bowden RA, Lanar DE, Heppner DG, Kellerman SA, Green LL, Production of Human Monoclonal Antibodies to the Plasmodium falciparum AMA-1 Protein, Paper to be presented at 51st ASTM Meeting to be held at Denver, CO, USA during 10-14 Nov 2002.
2. Haynes JD, Lanar DE, Dutta S, Lalitha PV, Barbosa A, Darko CA, Angov E, Lyon JA, Narum DL, Sim BKL, Moch JK, Malaria Growth Inhibition Assays (GIA) in Vaccine Candidate Evaluation: Roles of Suspension GIA and Reversal of Inhibition by Antigen, Paper to be presented at 51st ASTM Meeting to be held at Denver, CO, USA during 10-14 Nov 2002.
3. Cloning, Expression, Purification and Immunogenicity of Refolded Regions of Plasmodium falciparum AMA-1 Ectodomain in E. coli, Lalitha PV, Ware LA, Barbosa A, Dutta S, Moch JK, Vassell M, Haynes JD, and Lanar DE, Paper to be presented at 16th Annual Symposium of the Protein Society to be held in August 17-21, 2002 San Diego, California.
4. Lalitha PV, Ware LA, Barbosa A, Dutta S, Moch K, Vassel M Haynes JD, Lanar DE. Immunological characterisation of bacterially expressed Plasmodium falciparum AMA-1 Subdomain fragments. Proceedings of Keystone Symposia, Keystone, Colorado, USA, 3-8 March, 2002.
5. Dutta S, Barbosa A, Ware LA, Fileta BB, Lalitha PV, Moch JK, Vassell MA, Haynes JD, Lanar DE. Biophysical, biochemical and immunological comparison of a refolded malaria vaccine candidate Pf AMA-1/E, produced under GMP environment in two bacterial hosts. Proceedings of "Experimental Biology- Translating the Genome" during April 20-24, 2002, New Orleans, Louisiana, USA.
6. Lalitha PV, Ware LA, Moch K, Haynes JD, Dutta S, Barbosa A, Lanar DE. Expression, purification and immunological analysis of plasmodium falciparum ama-1 subdomains in bacteria, Proceedings of 50th ASTM Annual Meeting, Atlanta, Georgia, USA during 11-15, Nov 2001
7. Dutta S, Lalitha PV, Ware LA, Barbosa A, Moch K, Haynes JD, Vassell MR, Lanar DE. Purification and characterization of a refolded plasmodium falciparum apical membrane antigen-1 ectodomain produced under cGMP conditions for clinical use, Proceedings of 50th ASTM Annual Meeting, Atlanta, Georgia, USA during 11-15, Nov 2001.

Domestic

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* Include dates, names and locations of seminars.

1. Cloning, Expression and Immunological Characterization of Apical Membrane Antigen (AMA-1) Subdomain Fragments from P. falciparum, Immunology Department, CD&I, Walter Reed Army Institute of Research, on 11 September 2002.
2. Cloning, Expression and Immunological Studies of Apical Membrane Antigen (AMA-1) and its Subdomain Fragments from P. falciparum, Seminar during NRC Meeting at WRAIR during April 2002

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

Young Scientist Project, Department of Science and Technology, New Delhi, India for a Project entitled Structural and functional characterisation of some important malarial blood stage vaccine target antigens from Plasmodium falciparum Indian isolates.

14) *NEW POSITION TITLE*

Research Scientist

15) *NEW POSITION ORGANIZATION* Provide name and address of organization.

Tentatively-Department of Science and Technology, New Delhi (Sponsors); Exact laboratory is to be decided in two months.

16) *NEW POSITION STATUS / CATEGORY* Please indicate only one.

- | | |
|--|--|
| <input type="checkbox"/> Remain at Host Agency as Permanent Employee | <input type="checkbox"/> Administrative Position at US Government Laboratory |
| <input type="checkbox"/> Remain at Host Agency as Contract/Temporary Employee | <input type="checkbox"/> Research Position at Foreign Government Laboratory |
| Abbreviate Host Laboratory/Center | |
| <input type="checkbox"/> Research Position at Another US Government Laboratory | |

- ☐ Research/Teaching at US College/University
☐ Research/Teaching at Foreign College/University
☐ Research/Administration in Industry
☐ Research/Administration in Non-Profit Organization

- ☐ Postdoctoral Research
☒ Self Employed
☐ Other: specify

17) *APPRAISAL OF THE ASSOCIATESHIP PROGRAM* Please rate each of the following on a scale of 1 (poor) to 10 (excellent).

Your experience as a NRC Research Associate in this federal Laboratory

7 Short-term value: development of knowledge, skills, and research productivity

Comments:

I had the freedom to choose my project, plan and execute the way I wanted; hard work and earlier experience in this field helped me a lot to be very productive.

8 Long-term value: how your NRC Associateship award affected your career to date

Comments:

It was really a good exposure, it helped me to get more confidence in my abilities to do research. I could collaborate with some other projects/ laboratories such as Crystal structure elucidation of D I+II of AMA-1(BSI Proteomics Corporation, Gaithersburg, MD), Mapping of human monoclonal antibodies (Arnoldo Borbosa, WRAIR ; Medarex Corporation etc.) These experiences certainly helped me to improve my skills and will help to work more effectively on my return to India.

Administrative Support

8 Quality of the support you received from the federal Laboratory

9 Quality of the support you received from the NRC staff

Comments:

I am extremely thankful for the liberal support I received from NRC staff both from my Institute (Dr Sara Rothman's office) and also from Washington DC office. I never had any difficulty in finding solutions to my tiny problems.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT*

US Postal Service mailing address

Research Associateship Programs
National Research Council
500 Fifth Street, NW [GR 322A]
Washington, DC 20001

fax
202 - 334 - 2759

rap@nas.edu

website

www.national-academies.org/rap

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National Research Council
2001 Wisconsin Avenue, NW [GR 322A]
Washington, DC 20007

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Advisers to the Nation on Science, Engineering, and Medicine

Research Associateship Programs

FINAL REPORT

Enter information electronically in Layout view.

Return this form directly to the National Academies as an E-mail attachment, or print out and mail or fax.

1) Associate Last or Family Name		First Name	M.I.
Savransky		Vladimir	M
2) FORWARDING Address (to which your tax statement will be mailed)		FORWARDING Phone(s) and E-Mail (if known)	
5325 Randolph Rd. #2, Rockville, MD 20852		Phone: (301) 230-0035 Phone: (240) 476-6774 E-mail: vsavransky@yahoo.com	
3) Today's Date		Dates of Tenure	
February 3, 2003		from February 12, 2001 to February 11, 2003	
4) Agency	Laboratory or NASA Center	Division / Branch / Directorate	
AMRMC	WRAIR	Experimental Pathology	

5) Name of Research Associateship Programs Adviser

Jeenan Tseng, PhD

6) TITLE OF RESEARCH PROPOSAL

Mucosal Immune Response to Staphylococcal Enterotoxin B (SEB) Mutants Cloned into Lactobacillus casei

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Developing the new murine intranasal SEB toxic shock model.
- 2) Screening various SEB mutant proteins for superantigenicity, toxicity, and selecting safe mucosal vaccine candidate.
- 3) Studying immunogenicity and protective properties of selected candidates.
- 4) Developing a novel mucosal vaccine against SEB intoxication
- 5)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Developing and describing histopathology of murine TSST-1 induced toxic shock model.

9) PUBLICATIONS AND PAPERS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

1. V. Savransky, V. Rostapshov, D. Pinelis, Y. Polotsky, S. Korolev, K. Fegeding, J. Komisar, and J. Tseng. Murine Lethal Toxic Shock Caused by Intranasal Administration of Staphylococcal Enterotoxin B (2003). Toxicologic Pathology, 31(4).

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

1. D. Pinelis, V. Savransky, S. Korolev, J. Komisar, K. Fegeding, and J. Tseng. Immunogenicity of the Histidine-to-Tyrosine Staphylococcal Enterotoxin B Mutant in C3H/HeJ Mice. (Submitted to Vaccine)
2. V. Savransky, D. Pinelis, S. Korolev, J. Komisar, B. Ionin, K. Fegeding, and J. Tseng. Novel Intranasal Vaccine Candidate Protects Mice against Lethal Staphylococcal Enterotoxin B Challenge (Manuscript in preparation)
3. S. Korolev, D. Pinelis, V. Savransky, J. Komisar, P. Vogel, and K. Fegeding. Toxicity of the Staphylococcal Enterotoxin B (SEB) Mutants with Histidine-to-Tyrosine Substitutions. (Submitted to Toxicology)

10 PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH

Provide titles, inventors, and dates of applications.

n/a

11) **PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES**

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Experimental Pathology 2002, "Translating the Genome", New Orleans, LA, April 19-24, 2002

1. Savransky V, Pinelis D, Fegeding K, Polotsky Y, Komisar J, Tseng J. Lethal Toxic Shock Induced by Intranasal Inoculation of Staphylococcal Enterotoxin B (SEB) in Unmanipulated Mice. FASEB Journal. 2002; 16(5): A967.
2. Korolev S, Pinelis D, Savransky V, Fegeding K, Komisar J, Tseng J. Superantigenicity and Toxicity of Staphylococcal Enterotoxin B (SEB) Mutants with Histidine-to-Tyrosine Substitution. FASEB Journal. 2002; 16(5): A680.

Domestic

12) **SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES** Include dates, names and locations of seminars.

n/a

13) **PROFESSIONAL AWARDS RECEIVED DURING TENURE**

n/a

14) **POST-TENURE POSITION TITLE**

n/a

15) **POST-TENURE ORGANIZATION** Provide name and address of organization.

n/a

16) **POST-TENURE POSITION STATUS / CATEGORY** Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Remain at Host Agency as Permanent Employee | <input type="checkbox"/> Research/Teaching at US College/University |
| <input type="checkbox"/> Remain at Host Agency as Contract/Temporary Employee | <input type="checkbox"/> Research/Teaching at Foreign College/University |
| Abbreviate Host Laboratory/Center _____ | <input type="checkbox"/> Research/Administration in Industry |
| <input type="checkbox"/> Research Position at Another US Government Laboratory | <input type="checkbox"/> Research/Administration in Non-Profit Organization |
| <input type="checkbox"/> Administrative Position at US Government Laboratory | <input type="checkbox"/> Postdoctoral Research |
| <input type="checkbox"/> Research Position at Foreign Government Laboratory | <input type="checkbox"/> Self Employed |
| | <input checked="" type="checkbox"/> Other: specify n/a |

17) **APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM** Please rate each of the following on a scale of 1 (poor) to 10 (excellent).

Your experience as a National Academies Research Associate in this federal Laboratory

- 10** Short-term value: development of knowledge, skills, and research productivity

Comments:

- 8** Long-term value: how the National Academies Associateship award affected your career to date

Comments:

Administrative Support

- 7** Quality of the support you received from the federal Laboratory

- 10** Quality of the support you received from the Research Associateship Programs staff (Leave blank, if not applicable-- e.g., NIST)

Comments:

I have received high quality administrative support from both Laboratory and RAP stuff, including information, accomadation, and relocation.

18) **PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.**

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FINAL REPORT

Enter information electronically in Layout view.

Return this form directly to the NRC as an E-mail attachment, or print out and mail or fax.

1) Associate Last or Family Name Zhu		First Name Shuren	M.I.
2) FORWARDING Address (to which your tax statement will be mailed) 14110 Grand Pre Road #33, Silver Spring, MD 20906		FORWARDING Phone(s) and E-Mail (if known) Phone: 301-871-0032 Phone: 301-319-9645 E-mail: shuren.zhu@na.amedd.army.mil	
3) Today's Date October 7, 2002		Dates of Tenure from November 1, 2001 to October 31, 2002	
4) Agency AMRMC	Laboratory or NASA Center WRAIR	Division / Branch / Directorate Experimental Therapeutics	

5) NAME OF RESEARCH ADVISER

Ai Jeng Lin, Ph.D.

6) TITLE OF RESEARCH PROPOSAL

Design and Synthesis of Cysteine Proteinase Inhibitors as Potential Antimalarial Therapeutics

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) A novel class of peptidomimetic antimalarial agents has been discovered.
- 2) Compounds exhibited potent in vitro and in vivo activity against malarial parasites.
- 3)
- 4)
- 5)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

A novel class of peptidomimetic antimalarial agents has been discovered. The core structure of these compounds consists of a substituted 5-aminopyrimidone ring and a Michael acceptor side chain. These compounds exhibited potent in vitro growth inhibitory activity against both chloroquine sensitive (D-6) and chloroquine resistant (W-2) Plasmodium falciparum clones. This class of compounds exhibited weak to insignificant in vitro cytotoxicity against neuronal, macrophage, and colon cell lines. A scale-up synthesis has also been performed, gram quantities of these compounds has been made available for in vivo anti-malarial studies. Some selected compounds exhibited in vivo antimalarial activity at 40-160 mg/kg dosages.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Shuren Zhu, Thomas H. Hudson, Dennis E. Kyle, and Ai J. Lin, Synthesis and In Vitro Studies of Novel Pyrimidinyl Peptidomimetics as Potential Antimalarial Therapeutic Agents. Journal of Medicinal Chemistry, 2002, 45, 3491-3496.

b) Books, book chapters, other publications

None

c) Manuscripts in preparation, manuscripts submitted

None

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide titles, inventors, and dates of applications.

None

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

None

Domestic

Synthesis of Pyrimidinyl Peptidomimetics As Potential Antimalarial Therapeutics, Shuren Zhu and Ai J. Lin, presented at the 34th American Chemical Society Middle Atlantic Regional Meeting, Towson, Maryland, 2001.

12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars.

None

13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

None

14) NEW POSITION TITLE

Research Associate

15) NEW POSITION ORGANIZATION Provide name and address of organization.

WRAIR, 503 Robert Grant Avenue, Silver Spring, Maryland 20910

16) NEW POSITION STATUS / CATEGORY Please indicate only one.

- | | |
|--|---|
| <input type="checkbox"/> Remain at Host Agency as Permanent Employee | <input type="checkbox"/> Research/Teaching at US College/University |
| <input checked="" type="checkbox"/> Remain at Host Agency as Contract/Temporary Employee | <input type="checkbox"/> Research/Teaching at Foreign College/University |
| Abbreviate Host Laboratory/Center WRAIR | <input type="checkbox"/> Research/Administration in Industry |
| <input type="checkbox"/> Research Position at Another US Government Laboratory | <input type="checkbox"/> Research/Administration in Non-Profit Organization |
| <input type="checkbox"/> Administrative Position at US Government Laboratory | <input type="checkbox"/> Postdoctoral Research |
| <input type="checkbox"/> Research Position at Foreign Government Laboratory | <input type="checkbox"/> Self Employed |
| | <input type="checkbox"/> Other: specify _____ |

17) APPRAISAL OF THE ASSOCIATESHIP PROGRAM Please rate each of the following on a scale of 1 (poor) to 10 (excellent).

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10 Short-term value: development of knowledge, skills, and research productivity

Comments:

10 Long-term value: how your NRC Associateship award affected your career to date

Comments:

Administrative Support

10 Quality of the support you received from the federal Laboratory

10 Quality of the support you received from the NRC staff

Comments:

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT

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